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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/413,110	10/06/99	UNGER E	UNGR-1580

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DAVID A CHERRY ESQ
WOODCOCK WASHBURN KURTZ
MACKIEWICZ & NORRIS LLP
ONE LIBERTY PLACE 46TH FLOOR
PHILADELPHIA PA 19103

EXAMINER	
SHARAREH,S	
ART UNIT	**PAPER NUMBER**
1616	7

DATE MAILED: 06/06/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/413,110	Evan Unger
Examiner	**Group Art Unit**
Shahnam Sharareh	1616

☒ Responsive to communication(s) filed on *10/08/99, 5/16/00*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *63-67 and 75-115* is/are pending in the applicat

Of the above, claim(s) *88-93 and 98-107* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *63-67, 75-87, 94-97, and 108-115* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *5*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. The Amendment filed on May 16, 2000 has been entered. Accordingly, claims 1-62, and 68-74 have been canceled, and claims 75-115 have been added. Claims 63-67, and 75-115 are now pending.

Applicant's election of Group II in Paper No. 6 is acknowledged. Since Applicant did not traverse the restriction requirement, the instant election is considered without traverse and is hereby made FINAL.

Also, acknowledgment is made of Applicant's election of the species, wherein the vesicles comprise phospholipids, the gas or gaseous precursor comprise perfluorobutane, the thrombolytic agent comprise streptokinase, and the vesicle composition is administered at a rate of from 1 x ~~10^{-7} to about 3 x 10^{-3} cc gas/Kg-sec.~~ Accordingly, claims 88-93, 98-107 are withdrawn from further consideration by the Examiner, because they are directed to non-elected species.

This application contains claims drawn to an invention nonelected without traverse in Paper No. 6. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Priority

2. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The second application (which is called a continuing application) must be an application for a patent for an invention which is also disclosed in the first application (the parent or provisional application); the disclosure of the invention in the parent application and in the continuing application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *In re Ahlbrecht*, 168 USPQ 293 (CCPA 1971).

3. In the instant case, the U.S. application Serial No. 09/290,234, filed April 12, 1999, now pending, and the U.S. application Serial No. 08/666,129, filed June 19, 1996, now U.S. Patent No. 6,033,645 fail to teach a methods of lysing a thrombus utilizing a thrombolytic agent such as streptokinase and simultaneously using a ultrasound contrast agent containing a perfluorocarbon gas. Thus, the effective priority date used for the examination of the instant application is October 6, 1999.

Claim Rejections -- 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 63, 66, 75, 94-97 rejected under 35 U.S.C. 102(b) as being anticipated by Porter et al (Am Heart J 1996 Nov; 132(5):964-968 (abstract))

The instant claims are directed to methods of lysing a thrombus comprising (I) administering a thrombolytic agent to a patient, (ii) administering a vesicle composition

comprising an aqueous carrier, a gas or gaseous precursor, and vesicles comprising lipids, proteins or polymers to the patient (iii) and applying ultrasonic energy to the thrombus area, wherein the gas comprise a perfluorocarbon, and the thrombus is in a cardiac blood vessel.

Porter et al disclose a method of treating thrombosis comprising administering aqueous solution of dextrose 5% containing microbubbles comprising a polymeric wall made of albumin, and perfluorocarbon gas, (ii) administering a thrombolytic agent such as urokinase, (iii) and applying ultrasound simultaneously to achieve better thrombolysis (see abstract.) Thus, Porter et al meet the limitations set forth in the instant claims.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 63-67, 75-87, 94-97, 108-115 are rejected under 35 U.S.C. 103(a) as being unpatentable over Porter TR et al (Am Heart J 1996 Nov 132(5):964-968 abstract.) in view of Porter US Patent 5,648,098, and further in view of Schutt et al US Patent 5,626,833.

The instant claims are directed to methods of lysing a thrombus comprising (I) administering a thrombolytic agent to a patient, (ii) administering a vesicle composition comprising an aqueous carrier, a gas or gaseous precursor, and vesicles comprising lipids,

proteins or polymers to the patient (iii) and applying ultrasonic energy to the thrombus area, wherein the gas comprise a perfluorocarbon, and the thrombus is in a cardiac blood vessel.

The teachings of Porter et al (Am Heart J 1996 abstract) is discussed above. Therefore, it is settled in the art that administration of perfluorocarbon containing microbubbles improves the thrombolytic activity of agents used for such treatment methods.

Porter in US Patent 5,648,098 also teaches the effective use of perfluorocarbonated microbubbles alone at a rate of 0.0025-1ml/kg over about 1-25 minutes (which is roughly about 1.6×10^{-6} to 6×10^{-6} ml-kg/sec), wherein perfluorocarbon gas is perfluorobutane (see claims 1-5.)

Both teachings of Porter fail to disclose vesicles comprising phospholipids.

Schutt et al disclose various types of perfluorinated microbubbles for use as ultrasound contrast agent comprising phospholipid containing walls (see claims 1-10.) Schutt et al further indicate that the use of their perfluorocarbon containing compositions can enhance the thrombolytic activity of agent such as TPA or Streptokinase (see col 11, lines 18-30.)

The teachings of Porter and Schutt are viewed as being in the same field of endeavor because they all teach the enhancement of thrombolytic activity when administering perfluorinated microbubbles.

The policy of the US PTO is to give pending claims their broadest reasonable interpretation. The instant open-ended claims comprise and do not exclude any components or method steps essential to the operability of the cited prior arts. Furthermore, differences in ranges

will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such ranges (such as the instant rate of administration) is critical. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose . . . . the idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven , 626 F.2d 846, 205 USPQ 1069, 1072 (CCPA 1980) (citations omitted) Therefore, one ordinary skilled in the art would have been motivated at the time of invention to combine the teachings of Porter et al (Am Heart J abstract) and Porter US Patent 5,648,098, because he would have had a reasonable expectation of success in enhancing the lytic effects of thrombolytics such as streptomycin in treatment of thrombosis. Further, it is well within purview of an ordinary skilled artisan to optimize the rates of administration of the contrast agents that are disclosed by Porter in US Patent 5,648,098, and establish administration rates for the contrast agents of choice. Finally, modifying Porter's compositions as taught by Schutt and formulating phospholipid containing microbubbles to be used in Porter's method, would have also been obvious.

Information Disclosure Statement

The references EQ-ES, and EC-FS, as well as foreign patent documents WO 91/03267, WO 94/21301, WO 95/03835, WO 95/32005 were not provided by the Applicant and thus were not considered for this Office Action.

Conclusion

No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh, PharmD whose telephone number is (703) 306-5400. The examiner can normally be reached on Monday to Friday from 8:30 a.m. to 5:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Jose Dees can be reached on 703-308-4628. The fax phone number for this Group is 703-308-4556. Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is 703-308-1235.

sjs 5/31/00

S. MARK CLARDY
PATENT EXAMINER
GROUP ~~1200~~ 1616